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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,187	07/09/2003	Ann M. Lees	10797-004005	5109

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EXAMINER	
SKELDING, ZACHARY S	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/616,187	LEES ET AL.	
	Examiner	Art Unit	
	Zachary Skelding	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11,20-28,31-33,39-43,49-53,55,57,60,61,64,65 and 72-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *31-33* is/are allowed.

6)☒ Claim(s) *6,7,9-11, 20-21, 23-28, 39-43, 49-53, 55, 57, 72 and 73* is/are rejected.

7)☒ Claim(s) *8,22,60,61,64,65 and 74-77* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed May 3, 2006 has been entered.

   Claims 6-11, 20-23, 28, 31-33 and 43 have been amended.

   Claims 1-5, 12-19, 29, 30, 34-38, 44-48, 54, 56, 58, 59, 62, 63 and 66-71 have been canceled.

   Claims 72-77 have been added.

   Claims 6-11, 20-28, 31-33, 39-43, 49-53, 55, 57, 60, 61, 64, 65, and 72-77 are pending.

   Claims 6-11, 20-28, 31-33, 39-43, 49-53, 55, 57, 60, 61, 64, 65, and 72-77 are under examination as they read on antibodies that bind SEQ ID NOs: 7 and 43.

2. The rejections of record can be found in the previous Office Action, mailed November 3, 2005.

   This Office Action is in response to Applicant's amendment filed May 3, 2006.

   The text of those sections of Title 35 U.S.C. not included in this Office Action can be found in the previous Office Action.

3. The previous **objection** to the claims has been withdrawn in view of applicant's amendment to the claims.

   The previous **rejection under 35 U.S.C. § 101** has been withdrawn in view of applicant's amendment to the claims.

   The previous **rejection under 35 U.S.C. § 112, 2nd paragraph** has been withdrawn in view of applicant's amendment to the claims.

4. **Claims 9 and 23** stand rejected under **35 U.S.C. § 112, 1st paragraph** as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use an antibody fragment which is a heavy chain monomer, heavy chain dimer, heavy chain trimer, light chain chain monomer, light chain dimer, light chain trimer, and a dimer consisting of one heavy and one light chain, all of which bind LBP-2, for the reasons of record set forth in the previous Office Action. Moreover, **as a result of applicant's amendment to the claims, claims 6, 7, 10, 20, 21, including dependent claims 11, 24-28, 39-43, 49-53, 55, and 57, and newly added claims 72 and 73** are also rejected under **35 U.S.C. § 112, 1st paragraph.**

   Applicant's arguments have been considered but are not found convincing essentially for the reasons of record set forth in the previous Office Action.

Applicant argues that one of ordinary skill in the art would have been able to make and use the antibody fragments of claims 9 and 23 at the time the present application was filed, and that satisfaction of the enablement requirement only requires one of skill in the art be able to make and use such antibody fragments without undue experimentation and a reasonable expectation of success.

Applicant further argues that there is nothing in Hollinger to indicate that it would require undue experimentation to make and use the claimed antibody fragments and that Holliger confirms ***single variable domain antibodies*** were well known in the art.

However, page 1127, column 2 of Holliger, cited in the previous office action, teaches that "***despite early excitement concerning the functional activity of single V domains***, these fragments ***remained laboratory curiosities*** because they rarely retained the affinity of the partent antibody and were also poorly soluble and often prone to aggregation." This statement does ***not*** support applicant's contention that one of skill in the art would be able to make and use ***single variable domain antibodies*** without undue experimentation and a reasonable expectation of success.

Applicant also argues that "[t]he description of Hollinger of many different multivalent designs of antibodies confirms the enablement of claims 9 and 23 as directed to ***dimeric and trimeric forms of antibodies***."

However, the instant specification does not provide sufficient guidance to one of skill in the art to make the ***"dimeric and trimeric forms of antibodies"*** described by Holinger which include, as described on pages 1127-1128 and portrayed in Figure 1:

(a) "heavy chain dimer" antibodies, such as those that occur naturally in camelids and cartilaginous fish (although the "heavy chains" of such molecules differ markedly from heavy chains generated in other species, and these difference account for their unique structure, solubility and stability);

(b) multivalent single chain antibodies, such as the "diabody", which is made up of a "heavy chain dimer" **AND** a "light chain dimer", or the "triabody", which is made up of a "heavy chain trimer" **AND** a "light chain trimer"; and

(c) multivalent chemically modified Fab fragments, such as the "Fab_3", which is made up a "heavy chain trimer" **AND** a "light chain trimer".

The instant specification does not disclose or exemplify the production of antibodies via immunization of a camelid or cartilaginous fish, or by "camelizing" an anti-LBP2 antibody heavy chain domain. Moreover, the instant specification does not even mention single chain antibodies, much less how to connect heavy and light chains using a linker of the appropriate length such that a molecule made up of a "heavy chain dimer" **AND** a "light chain dimer" (diabody), or a molecule made up of a "heavy chain trimer" **AND** a "light chain trimer" (triabody) will be formed. Also, the instant specification does not teach chemical cross-linking of Fab fragments to create a molecule made of a "heavy chain trimer" **AND** a "light chain trimer" (Fab_3).

5. **Claims 9 and 23** stand rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had ***possession*** of antibody fragment which is a heavy chain monomer, heavy chain dimer, heavy chain trimer, light chain chain monomer, light chain dimer, light chain trimer, and a dimer consisting of one heavy and one light chain, all of which bind LBP-2, for the reasons of record set forth in the previous Office Action. Moreover, **as a result of applicant's amendment to the claims, claims 6, 7, 10, 20, 21, including dependent claims 11, 24-28, 39-43, 49-53, 55, and 57, and newly added claims 72 and 73** are also rejected under **35 U.S.C. § 112, 1st paragraph.**

Applicant's arguments have been considered but are not found convincing essentially for the reasons of record set forth in the previous Office Action and in the preceding section.

There is insufficient written description in the specification as-filed for an antibody fragment which is a heavy chain monomer, heavy chain dimer, heavy chain trimer, light chain chain monomer, light chain dimer, light chain trimer, and a dimer consisting of one heavy and one light chain that binds LBP-2. The instantly claimed antibody fragments lack a common structure essential for their function, and the claims do not require any particular structure basis be shared by the instant antibody fragments. The genus of the instantly claimed antibody fragments is therefore extremely large.

It does not appear based upon the instant specification that Applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the extensive variation permitted within the claimed genus.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial

variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP 2163 II.A.3a.ii.

"Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997).

The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 1115).

6. Claims 31-33 are allowable. Claims 8, 22, 60, 61, 64, 65 and 74-77 are objected to for being dependent on a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
July 17, 2006

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TC 1600
7/18/06